REMARKS/ARGUMENTS

Claims 1-30 are pending. Claims 3-10 and 15-22 are withdrawn. Claims 1, 2, 11-14 and 23-30 are rejected.

Applicants have amended claims 1 and 12 to recite elected subject matter and to correct a typographic error, canceled claims 3-10 and 15-22 without prejudice, and added new claim 31. Applicants have also amended the specification to correct a typographical error. None of the amendments introduce new matter.

Applicants respectfully request withdrawal of the finality of this rejection. The Examiner states that the Rajagopalan Declaration, included as part of applicants' previous Amendment, "was not found in the file", yet applicants received and include a copy of their postcard stamped by the United States Patent and Trademark Office, specifically listing the Rajagopalan Declaration. Applicants also include a copy of the previously filed Rajagopalan Declaration for convenience. The Declaration previously filed, but not considered by the Examiner, was by an inventor and included copies of pages from scientific references, and hence constituted more than "mere allegations".

Applicants have retained the Examiner's paragraph number designations for convenience in the following response, and respectfully request reconsideration for the following reasons.

3-4. Applicants have canceled claims 3-10 and 15-22 without prejudice. Applicants have also amended claims 1 and 12 to recite elected subject matter.

CLAIM REJECTIONS UNDER 35 U.S.C. § 112

Claims 1, 2, 11-14 and 23-23 are rejected under 35 U.S.C. § 112 ¶2 as indefinite.

5-8. Applicants respectfully disagree that the claims are indefinite. In addition to the previous Amendment filed on February 19, 2003, and the resubmission of the Rajagopalan Declaration and references cited therein, applicants provide the following in further support.

Considering the four indefiniteness rejections together, as the Examiner did, it is the Examiner's position that the epitope, E, must be an univalent radical. Applicants respectfully disagree, as analyzed below. The Examiner further questions the chemical structures of radical E and whether E is an antibody or only a short peptide. The Examiner additionally states that the phrase "carbohydrate receptor-binding molecule" is indefinite and asks "How would one know if any molecule E bound to such a receptor without checking all such receptors?"

Applicants respectfully assert that it is well known that an epitope, E, is an antigenic determinant and that binding of the antigen to a receptor, like the binding of a substrate to an enzyme, is through weak noncovalent forces, which include hydrophobic and hydrogen bonds, van der Waals forces and/or ionic forces. The epitope may be either the whole protein or a protein fragment. Alberts et al., *Molecular Biology of the Cell,* 2nd Ed., chapter 18, pp. 1006, 1016-1017, and 1030, Garland Publishing, Inc., New York, 1989; Kuby, *Immunology*, W.H. Freeman and Co., New

York, 1992, pp. 78-83; Stryer, Biochemistry, 3rd Ed., W.H. Freeman & Co., New York, 1988, pp. 62 and 890-893 (copies of each attached).

More specifically, for example, Rohrer et al. (Science 282 (1998), pp. 737-740) lists and describes particular somatostatin receptor agonists ("In receptor-ligand binding assays, short peptide analogs of somatostatin, including MK-678 and octreotide, display selectivity for the ss2 receptor." p. 738). This is only one example; other examples of these specific compounds are Cayanis et al. (J.Biol.Chem 261 (1986), pp. 5094-5103) describing antibodies which bind to glucocorticoid receptor; Licha et al. (SPIE 3600 (1999), pp.29-35); Ballou et al. (Cancer Immunology and Immunotherapy 41 (1995) pp. 257-263); Pèlegrin et al. (J. Cell Pharmacol. 3 (1992, pp. 141-145) describing conjugation of biomolecules with dyes (copies attached). These clearly demonstrate that one skilled in the art would know the meaning of the terms "epitope" and "carbohydrate receptor binding molecule" and their mechanism of action, and how to form a target specific dye molecule without "checking" all receptors. Furthermore, the Markush group of claim 1 restricts E to particular somatostatin, carbohydrate, steroid, etc., receptor binding molecules.

The Examiner also questions the meaning of "associated with biomolecules" in applicants definition of "E" and whether the synthetic biomolecules listed in lines 11-13, page 13 are "E".

Applicants describe that an epitope may be "associated with biomolecules" (page 12, lines 18-19) and that the biomolecules may include "synthetic polymers". Hence, applicants respectfully assert that the synthetic biomolecules are not epitopes but are "associated" with the epitope. The term "associated" is used

conventionally to mean connected to or united with. It is well known in the art that macromolecules, such as proteins or protein fragments may have another component "associated" with it thus forming a multicomponent complex. The association may be of various types such as hydrophobic or covalent as in lipoproteins and glycoproteins, respectively. This type of association between biomolecules and synthetic biomolecules is well known (*see, e.g.,* Textbook of Biochemistry with Clinical Correlations, T.M. Devlin, John Wiley & Sons, New York, 1992, at least on pp. 67 and 70-71; Stryer at least on p. 298).

9. Applicants respectfully disagree that there is no antecedent basis for the limitation in claim 11 and that claim 11 is broader in scope than the parent claim.

E is recited in claim 1, and is further limited by its association with a biomolecule, as recited in claim 11. Applicants have previously described the meaning of "associated with a biomolecule."

10. The Examiner finds that claims 1, 2, 11-14, 23-30 are not enabled for other E binding molecules except for E being dihydroxyindolecarboxylic acid or the peptide cytate, and that locating "all possible epitope sites on these antibodies is an impossible task." Applicants respectfully disagree.

In addition to applicants' previous arguments, the term "epitope" denotes specific binding sites in a molecule, i.e., the site at which actual intermolecular interaction takes place between antigen-antibody, ligand-receptor, and enzyme-substrate. In some cases, only a small part of the molecule participates in binding,

while in others the entire molecule may participate. In addition, applicants cite several references in the specification as examples of methods well known in the art of coupling diagnostic and radiotherapeutic agents to biomolecules (page 13, lines 12, to page 14, line 7). One skilled in the art would know which epitope to choose and how to attach it to, for example, a dye-sulfenate, or any other effector molecule and target it to the site of interest.

11. In reference to claims 1, 2, 11-14, 23-30, the Examiner finds that the specification contains subject matter not described in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, specifically, the meaning of the phrases "somatostatin binding molecule"..."carbohydrate binding molecule." Applicants respectfully disagree.

As shown in the arguments for paragraphs 5-10, applicants' composition, compound and use of is adequately described and enabled in the specification and incorporates methods, as known in the art, for the coupling of the dye with biomolecules.

12. In reference to claims 12-14 and 23-30, it is the Examiner's position that while the specification is enabling for the specific diseases listed, the specification does not reasonably provide enablement for treating every target tissue.

Applicants have added new claim 31 to recite specific target tissues for the phototherapeutic procedure. For example, if the disease is breast cancer, one

would target the estrogen receptor for breast cancer imaging by choosing any commercially available estradiol derivative and covalently attach a dye molecule at the 7, 11, or 17 positions by using standard bioconjugate chemistry procedures, administer the conjugate to the patient for localization to the tumor site, and perform imaging or therapeutic procedures.

CONCLUSION

For the foregoing reasons, applicants respectfully request that all of the rejections have been overcome and a Notice of Allowance is respectfully requested.

Applicants believe that no fees are due. However, should any fees or surcharges be deemed necessary, the Examiner is authorized to charge fees or credit any overpayment to Deposit Account No. 23-3000.

The Examiner is invited to telephone applicants' undersigned representative if there are any questions.

Respectfully submitted,

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